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(54) Preparation of recombinant factor VIII in a protein free medium

(57) Recombinant Factor VIII can be produced in relatively large quantities on a continuous basis from mammalian cells in the absence of any animal-derived proteins such as albumin by culturing the cells in a protein free medium supplemented with polyol copolymers, preferably in the presence of trace metals such as copper. In very preferred embodiments, the medium includes a polyglycol known as Pluronic F-68, copper sulfate, ferrous sulfate/EDTA complex, and salts of trace metals such as manganese, molybdenum, silicon, lithium and chromium.

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EUROPEAN SEARCH REPORT

Application Number

EP 98 10 6133

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	EP 0 534 383 A (CHEMO SERO THERAPEUT RES INST ;TEIJIN LTD (JP)) 31 March 1993 (1993-03-31) * page 6, line 39 - line 44 * ---	1-3, 10-15	C07K14/755 C12N5/02 C12P1/00
Y	US 4 767 704 A (CLEVELAND WILLIAM L ET AL) 30 August 1988 (1988-08-30) * column 7 - column 8; claims 2,3 * ---	4-9	
X	EP 0 306 968 A (CHEMO SERO THERAPEUT RES INST ;TEIJIN LTD (JP)) 15 March 1989 (1989-03-15) * page 11, line 17 - page 12, line 30; claims 22-26 * ---	1,2, 10-15	
A	BIHOREAU, N. ET AL.: "Copper-atom identification in the active and inactive forms of plasma-derived FVIII and recombinant FVIII-delta II." EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 222, no. 1, 15 May 1994 (1994-05-15), pages 41-8, XP002113329 * the whole document * ---	4	TECHNICAL FIELDS SEARCHED (Int.Cl.6)
A	US 4 440 679 A (FERNANDES PETER M ET AL) 3 April 1984 (1984-04-03) * see whole document, particularly the summary of the invention (columns 3-4) * ---		C07K C12N C12P
A	US 5 024 947 A (INLOW DUANE ET AL) 18 June 1991 (1991-06-18) * see whole document, particularly examples 1-3,6,9 and claims 7-9 * ---		
		-/-	
The present search report has been drawn up for all claims			
Place of search	Date of completion of the search		Examiner
THE HAGUE	26 August 1999		Smalt, R
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background C : non-written disclosure P : intermediate document			
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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	EP 0 274 445 A (MEDI CULT AS ;GEA FARMACEUTISK FABRIK AS (DK)) 13 July 1988 (1988-07-13) * page 4, line 2 - line 5; claims 2,6,10,16,17 * -----		
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)
The present search report has been drawn up for all claims			
Place of search	Date of completion of the search	Examiner	
THE HAGUE	26 August 1999	Smalt, R	
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EP 98 10 6133

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26-08-1999

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0534383	A	31-03-1993	AU 663888 B AU 2530492 A JP 5268968 A NZ 244448 A US 5693499 A	26-10-1995 25-03-1993 19-10-1993 22-12-1994 02-12-1997
US 4767704	A	30-08-1988	NONE	
EP 0306968	A	15-03-1989	JP 3087173 A AT 97957 T AU 2200388 A DE 3885983 D DE 3885983 T ES 2061582 T KR 9512804 B	11-04-1991 15-12-1993 16-03-1989 13-01-1994 23-06-1994 16-12-1994 21-10-1991
US 4440679	A	03-04-1984	AT 30296 T CA 1187410 A DE 3176491 A DK 98681 A, B, EP 0035204 A JP 1980554 C JP 6011702 B JP 56139422 A US 4623717 A	15-11-1987 21-05-1985 26-11-1987 06-09-1981 09-09-1981 17-10-1995 16-02-1994 30-10-1981 18-11-1986
US 5024947	A	18-06-1991	AT 105856 T AU 2126688 A CA 1309679 A DE 3889665 D DE 3889665 T EP 0380495 A IE 64262 B JP 3500602 T WO 8901028 A	15-06-1994 01-03-1989 03-11-1992 23-06-1994 03-11-1994 08-08-1990 26-07-1995 14-02-1991 09-02-1989
EP 0274445	A	13-07-1988	AT 92098 T AU 596491 B AU 1011588 A CA 1321961 A DE 3882540 A DE 3882540 T DK 678687 A FI 875793 A, B, IT 1215675 B JP 1964694 C	15-08-1993 03-05-1990 14-07-1988 07-09-1993 02-09-1993 18-11-1993 10-07-1988 10-07-1988 22-02-1990 25-08-1995

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The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

26-08-1999

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0274445 A		JP 6097996 B	07-12-1994
		JP 63279786 A	16-11-1988
		JP 2524313 B	14-08-1996
		JP 6292570 A	21-10-1994
		US 5045467 A	03-09-1991
		US 5045454 A	03-09-1991

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